**EXHIBIT 1**

The central nervous system then forms a closed tubular structure with a narrow caudal portion, the **spinal cord**, and a much broader cephalic portion characterized by a number of dilatations, the **brain vesicles** (see "Central Nervous System," Chapter 20).

By the time the neural tube is closed, two other ectodermal thickenings, the **otic placode** and the **lens placode** become visible in the cephalic region of the embryo (fig. 5-6*B*). During further development, the otic placode invaginates and forms the **otic vesicle**, which will develop into the structures needed for hearing and maintenance of the equilibrium (see "Ear," Chapter 17). At approximately the same time, the **lens placode** appears. This placode also invaginates and during the fifth week forms the **lens** (see "Eye," Chapter 18).

In general terms it may be stated that the ectodermal germ layer gives rise to those organs and structures that maintain contact with the outside world: (1) the central nervous system; (2) the peripheral nervous system; (3) the sensory epithelium of ear, nose, and eye; and (4) the epidermis, including hair and nails. In addition it gives rise to: the subcutaneous glands; the mammary gland; the pituitary gland; and the enamel of the teeth.

## Derivatives of Mesodermal Germ Layer

Since the external contours of the embryo are greatly influenced by the formation of the **somites**, a series of mesodermal tissue blocks found on each

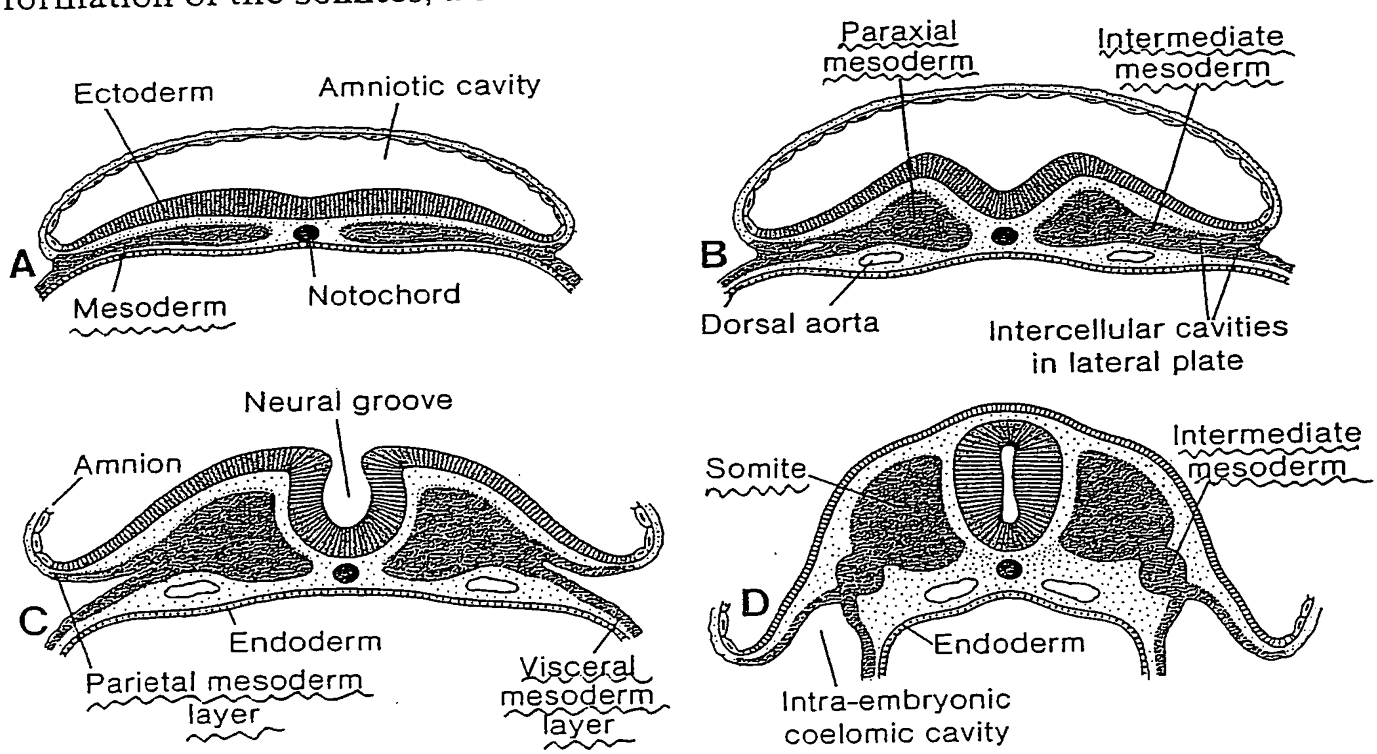


**Figure 5-7.** Transverse sections showing the development of the mesodermal germ layer. *A*, Day 17; *B*, day 19; *C*, day 20; *D*, day 21. The thin mesodermal sheet gives rise to the paraxial mesoderm (the future somites), the intermediate mesoderm (the future excretory units), and the lateral plate, which is split into the parietal and visceral mesoderm layers lining the intra-embryonic coelomic cavity.

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side of the neural tube, the development and differentiation of these structures will be discussed briefly.

Initially the cells of the mesodermal germ layer form a thin sheet of loosely woven tissue on each side of the midline (fig. 5-7*A*). By about the 17th day, however, the cells close to the midline proliferate and form a thickened plate of tissue, known as the **paraxial mesoderm** (fig. 5-7*B*). More laterally, the mesoderm layer remains thin and is known as the **lateral plate**. With the appearance and coalescence of intercellular cavities in the lateral plate, this tissue is divided into two layers (fig. 5-7*B*, *C*): (1) a layer continuous with the mesoderm covering the amnion, known as the **somatic** or **parietal mesoderm layer**; and (2) a layer continuous with the mesoderm covering the yolk sac, known as the **splanchnic** or **visceral mesoderm layer** (fig. 5-7*C*, *D*). Together, these layers line a newly formed cavity, the **intra-embryonic coelomic cavity**, which, on each side of the embryo, is continuous with the extraembryonic coelom. The tissue connecting the paraxial mesoderm and the lateral plate is known as the **intermediate mesoderm** (fig. 5-7*B*, *D*).

X. By the end of the third week the paraxial mesoderm breaks up into segmented blocks of epithelioid cells, the **somites**. The first pair of somites arises in the cephalic part of the embryo at about the 20th day of development. From here new somites appear in craniocaudal sequence, approximately three per day, until at the end of the fifth week 42 to 44 pairs are present (figs. 5-4 and 5-6).[1] These are 4 occipital, 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 8 to 10 coccygeal pairs. The first occipital and the last 5 to 7 coccygeal somites later disappear. During this period of development the age of the embryo is expressed in the number of somites, and Table 5-1 represents the approximate age of the embryo correlated to the number of somites.[2, 3]

## DIFFERENTIATION OF THE SOMITE

X. By the beginning of the fourth week the epithelioid cells forming the ventral and medial walls of the somite lose their epithelial shape, become polymorphous, and migrate toward the notochord (fig. 5-8*B*). These cells, collectively known as the **sclerotome**, form a loosely woven tissue known as **mesenchyme** or **young connective tissue**. They will surround the spinal cord and notochord to form the vertebral column (see "Skeletal System," Chapter 9).

The remaining dorsal somite wall, now referred to as the **dermatome**, gives rise to a new layer of cells, (fig. 5-8*C*) characterized by pale nuclei and darkly stained nucleoli. These cells fail to divide once they are laid down.[4] The tissue so composed is known as the **myotome**. Each myotome provides the musculature for its own segment (see "Muscular System," Chapter 10).

After the cells of the dermatome have formed the myotome, they lose their epithelial characteristics and spread out under the overlying ectoderm (fig.

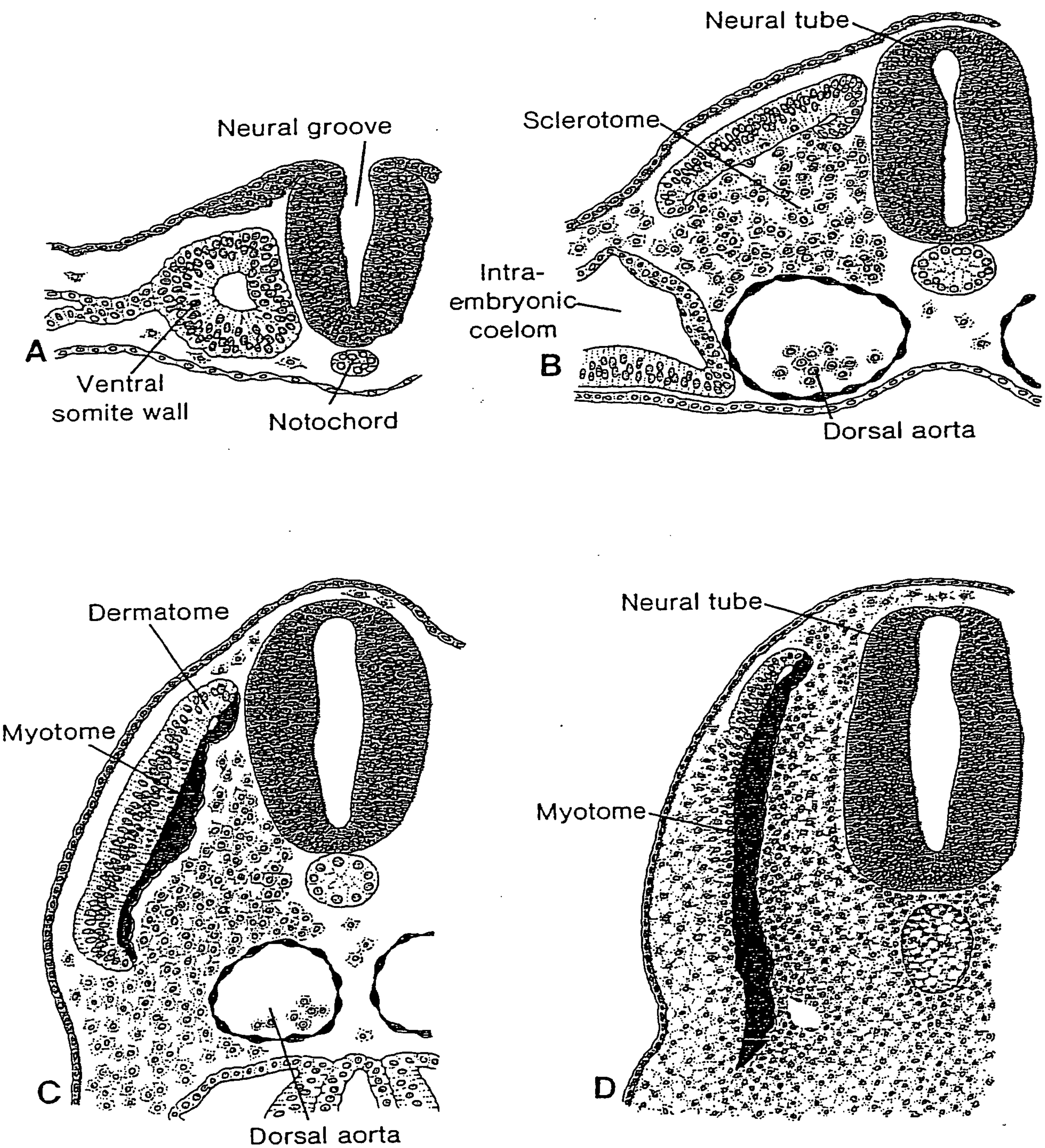


**Figure 5-8.** Successive stages in the development of the somite. *A*, The mesoderm cells are arranged around a small cavity. *B*, The cells of the ventral and medial walls of the somite lose their epithelial arrangement and migrate in the direction of the notochord. These cells are collectively referred to as the sclerotome. *C*, The dorsal somite wall gives rise to a new cell layer, the myotome. *D*, After extension of the myotome in ventral direction, the dermatome cells lose their epithelial configuration and spread out under the overlying ectoderm to form the dermis.

5-8*D*). Here they form the **dermis** and subcutaneous tissue of the skin (see "Integumentary System," Chapter 19). Hence, each somite forms its own **sclerotome** (the cartilage and bone component), its own **myotome** (providing the segmental muscle component), and its own **dermatome**, the segmental skin component. As will be seen later, each myotome and dermatome has its own segmental nerve component.

## INTERMEDIATE MESODERM

This tissue, which temporarily connects the paraxial mesoderm with the lateral plate (fig. 5-7*D*), differentiates in a manner entirely different from that of the somites. In the cervical and upper thoracic regions it forms

Table 5-1. **Number of Somites Correlated to Approximate Age in Days**

| Approx. Age | No. of Somites | Approx. Age | No. of Somites |
|---|---|---|---|
| *days* | | *days* | |
| 20 | 1–4 | 25 | 17–20 |
| 21 | 4–7 | 26 | 20–23 |
| 22 | 7–10 | 27 | 23–26 |
| 23 | 10–13 | 28 | 26–29 |
| 24 | 13–17 | 30 | 34–35 |

segmentally arranged cell clusters (the future **nephrotomes**), whereas more caudally it forms an unsegmented mass of tissue, known as the **nephrogenic cord**. From this partly segmented, partly unsegmented intermediate mesoderm develop the excretory units of the urinary system (see fig. 15-2).

## PARIETAL AND VISCERAL MESODERM LAYERS

These two layers line the intra-embryonic coelom (figs. 5-7*C*, *D* and 5-9*A*). The parietal mesoderm together with the overlying ectoderm will form the lateral and ventral body wall. The visceral mesoderm and the embryonic endoderm will form the wall of the gut (fig. 5-9*B*). The cells facing the coelomic cavity will form thin membranes, the **mesothelial** or **serous membranes**, which will line the peritoneal, pleural, and pericardial cavities (fig. 5–9*B*) (See "Body Cavities and Serous Membranes," Chapter 11).

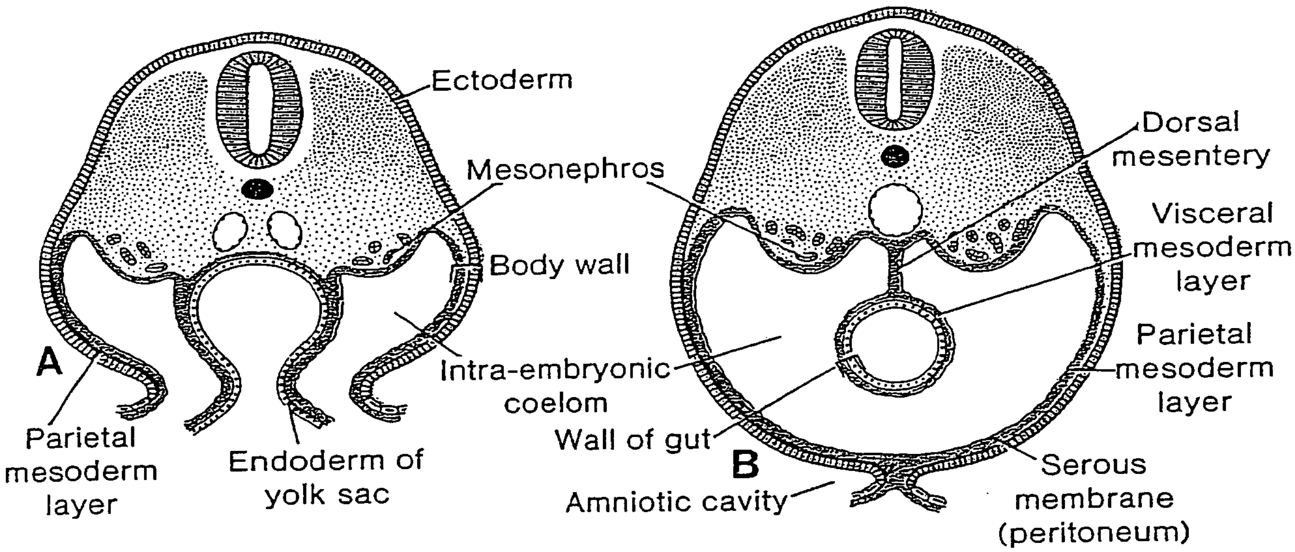


**Figure 5-9.** *A*, Transverse section through a 21-day embryo in the region of the mesonephros. Note the parietal and visceral mesoderm layers. The intra-embryonic coelomic cavities communicate with the extra-embryonic coelom or chorionic cavity. *B*, Section at the end of the fourth week. The parietal mesoderm and the overlying ectoderm form the ventral and lateral body wall. Note the peritoneal or serous membrane.

## BLOOD AND BLOOD VESSELS

At about the beginning of the third week mesoderm cells located in the visceral mesoderm of the wall of the yolk sac differentiate into blood cells and blood vessels. These cells, known as the **angioblasts**, form isolated clusters and cords (**angiogenetic cell clusters**), which gradually become canalized by confluence of intercellular clefts (fig. 5-10). The centrally located cells then give rise to the primitive blood cells, while those on the periphery flatten and form the **endothelial cells** lining the **blood islands** (fig. 5-10*B*, *C*). The blood islands approach each other rapidly by sprouting of

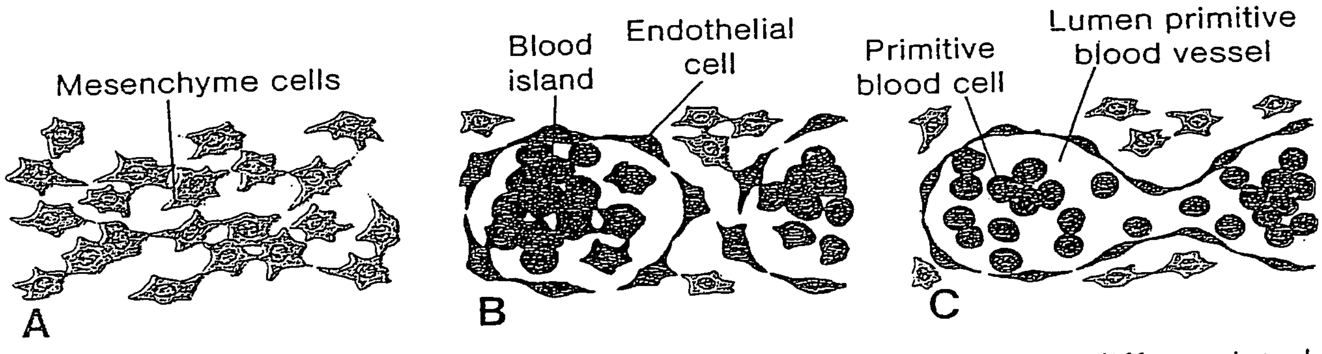


**Figure 5-10.** Successive stages of blood vessel formation. *A*, Undifferentiated mesenchyme cells. *B*, Blood island formation. *C*, Primitive capillary. Note the differentiation of mesenchymal cells into the primitive blood cells and the endothelial cells.